LMOs: TREASURE CHEST OR PANDORA'S BOX?

Biotechnology is beginning to transform agriculture across the globe. After thousands of years of traditional plant and animal breeding, and centuries of mechanization and chemical application, genetic research has opened a Pandora's box of living modified organisms (LMOs) designed to improve the productivity and efficiency of commercial agriculture. A multitude of transgenic crops and animals is now being introduced into commerce by biotechnology companies, and nations are puzzling out how to appropriate the benefits and manage the risks.

American biotechnology companies and agencies are the leading proponents of using LMOs. They claim that two decades of costly and careful research and several years of field testing in the United States prove that the LMOs being offered are a safe and effective means of improving productivity, reducing dependency on toxic chemicals, preventing environmental and health hazards, enhancing nutrition, achieving a reliable food supply for burgeoning populations in poorer countries, and promoting sustainable growth.

In their new book, *Agricultural Biotechnology and the Environment*, professors Sheldon Krimsky and Roger Wrubel of Tufts University assess the emerging universe of LMOs and divide it into several broad categories including:

- **herbicide-resistant crops** (such as new strains of corn, soybeans, and potatoes) in which new genes are introduced to diminish plant sensitivity to chemical herbicides, or to detoxify the herbicides;
- **insect-resistant crops** (such as new strains of corn, soybeans, and potatoes) in which the introduced genes, most commonly from *Bacillus thuringiensis* (Bt), kill specific insect pests that ingest the Bt without causing toxic or other harmful effects on nontarget species;
- **disease-resistant crops** (such as alfalfa, squash, corn, and potatoes) in which the new genes provide antifungal properties and other defenses against plant pathogens;
- **product-producing crops** in which the new genes enable plants to produce more nutritious or attractive foods (Calgene's Flavr Savr tomato), serums and vaccines (W.R. Grace's modified potato and tobacco plants), and oils for industrial use (new strains of rapeseed);
- **biopesticides,** which thus far involve release-modified forms of Bt in field applications to kill targeted pest species such as the European corn borer and the Colorado potato beetle, and which may soon include virulent strains of baculoviruses;
- **productivity-enhancing bacteria** such as nitrogen-fixing bacteria (to improve soil fertility) and frost-inhibiting bacteria;
- **animal growth hormones** to produce leaner meat for health-conscious consumers, or more productive animals (for example, using bovine somatotropin to increase milk production); and
- **transgenic animals,** created by introducing foreign DNA into fertilized eggs, to provide leaner meat, carry human disease for health research, or function as bioreactors in "pharming" for therapeutic products (such as Genzyme Transgenics' goat capable of producing BR-96, an experimental anticancer drug).

To develop such LMOs and introduce them into commerce, American companies must comply with a detailed framework of federal biosafety requirements that use risk assessment and risk management methods. The biosafety requirements range from containment of certain LMOs for research in secure laboratories to subsequent procedures for the assessment, approval, and monitoring of field releases. Since most LMOs intended for agricultural use ultimately require their release into the environment outside the lab, field test requirements are the most critical feature of the biosafety review process. Depending on the type of biotechnological product involved, regulatory authority of the United States Department of Agriculture, the Environmental Protection Agency, or the Food and Drug Administration applies to and governs company testing and introduction of agricultural LMOs into commerce.

In the past five years, over 2,000 field tests of LMOs at over 8,000 carefully selected sites in the United States have been approved and conducted without a single reported adverse or even unpleasant impact on the environment or public health, according to officials at the USDA. This far surpasses the total experience of all other nations, according to biotech industry and agency officials, and should provide considerable assurance to other nations that LMOs offered by American firms can be safely managed.

Concerns About LMOs

Genetically modified organisms that are not intended for agriculture but are used for research or development purposes, such as transgenic mice or bacteria, are subject to "contained use" requirements in the United States and the European Union countries. Such requirements are intended to prevent accidental release of LMOs, which could present an immediate or delayed hazard to health or the environment, and are risk-based and somewhat variable. Some containment measures used include physical and chemical barriers, engineering controls, negative air pressure, spill containment equipment, and treatment of wastes prior to off-site disposal. These measures are reinforced by requirements for employee training, protective equipment and decontamination facilities, emergency plans and practice codes, record-keeping and reporting, and biosafety oversight and accountability. By far the larger controversy deals with genetically modified organisms and agriculture.

Despite experience and claims about LMO benefits and safety, American companies and policymakers face dogged opposition as they promote the introduction of LMOs into commercial agriculture at home and abroad. Opponents challenge the scientific adequacy of American field testing for biosafety and company claims that LMOs ensure greater productivity. Many also contend that commercial use of LMOs will cause environmental and socioeconomic disruptions and undermine the self-reliance of developing nations.

For example, Jane Rissler and Margaret Mellon of the Union of Concerned Scientists, in their recent book, *The Ecological Risks of Engineered Crops*, raise questions about environmental risks. Although finding that "most genetically engineered organisms will not be harmful," they oppose unregulated commercial use on the grounds that American field testing for biosafety has been short-term and small-scale, and is even waived as a requirement for certain transgenic plants. Although the small field test sites have been carefully selected and monitored to minimize transgenic interbreeding with wild plant relatives and other undesirable consequences, these precautionary measures are not likely to be followed in developing nations at much larger commercial sites covering millions of acres. In addition, they say, the American test sites do not match likely commercial sites abroad in terms of ecological conditions, biodiversity, plant relatives with interbreeding potential, and natural events such as floods which can transport seeds to more vulnerable off-site regions.

Thus, Rissler and Mellon contend that American field testing offers little, if any, assurance of biosafety to other nations and, drawing on ecological principles, point to several risk scenarios:

- **gene flow**, in which new genes for insect, disease, or herbicide resistance flow to wild plant relatives and weeds, causing agricultural and ecological havoc unless effective controls are available and affordable;
- **harms to nontarget species** arising, for example, from new gene products with toxic qualities being ingested by birds and other feeders in the regions where such LMOs are cultivated;
- **cascading effects** on an ecosystem triggered by the introduction of LMOs, such as pests developing resistance over time to Bt in transgenic plants, or being deflected to other food sources; and
- **loss of biological diversity**, arising from LMO displacement of other species, with particular regard for those developing nations that possess great concentrations of crop diversity but lack infrastructure and expertise for preventing the loss.

Biotechnology companies and agencies draw on biosafety experience to dispute such contentions and argue that any residual risks are manageable. Conflicts over certain LMOs have also become quite intense, with both sides using various tactics to win over public perception and trigger market forces.

The newest conflict involves evidence of gene flow from an herbicide-resistant rapeseed that was engineered by Germany's AgroEvo GmbH for enhanced production of canola oil. According to a report by Danish researcher Thomas Mikkelsen and colleagues at the Riso National Laboratory in Roskilde, published in the 7 March 1996 issue of *Nature*, the herbicide-resistant genes quickly flowed to a wild plant relative through cross-breeding, and produced fertile offspring that are now herbicide-resistant as well. According to environmental and consumer groups, this study demonstrates that LMOs pose gene flow risks when plant relatives are nearby, that current agency oversight for biosafety is scientifically and legally inadequate to prevent such occurrences, and that the biotechnology mantra that "hybrids don't survive, so don't worry" is wrong.

However, Richard Godown of the Biotechnology Industry Association (BIO), which includes over 500 companies, government centers, and academic institutions in over 20 countries, describes the Danish study as "a propagation deliberately done in the laboratory which was then theoretically extrapolated to natural conditions," and believes that such gene flows in nature can be prevented by careful site selection for commercial agriculture, buffer zones, and other risk management methods.

Val Geddings, international team leader for the USDA's Animal and Plant Health Inspector Service, adds that the gene flow finding has been improperly described as an "unpleasant surprise," when in fact, it was well-known beforehand that rapeseed genes flow to certain weedy relatives without serious environmental consequences, whether the plant was traditionally bred or recombinant, as is the case with broccoli and cauliflower genes. Nor was it an adverse outcome according to Geddings, because the gene flow from the recombinant plant posed no greater environmental risk than the gene flow from its traditionally bred counterpart. As for the consequence of herbicide-resistant weeds, "one answer is to switch to another herbicide," he said.

In addition to environmental opposition, commercial use of LMOs is also resisted on grounds that it will cause major socioeconomic dislocations, particularly in developing nations where the initial impact would involve displacement of small family farms by more efficient, high-tech corporate agriculture. Some say a subsequent domino effect could include the erosion of traditional village culture, unemployment for the unskilled, and growing dependence on foreign interests and experts for food supply. Concurrently, native populations and their environments would become the subjects of further research to fine-tune the safer or more productive use of LMOs without adequate safeguards. Eventually, opponents worry that multinational firms from the United States or other developed nations could capture other local enterprises in the food production system, such as seed suppliers, shippers, distributors, brokers, processors, and retailers through acquisition, joint venture, or various forms of strategic alliance.

Although these concerns may seem to be merely another variation on the familiar tension between developed and developing nations, there is evidence in various regions of the United States that at least some of

these socioeconomic impacts can and do flow from corporate entry into local agriculture.

Environmental and consumer organizations in developed nations share these socioeconomic concerns, and many developing nations share their ecological concerns regarding biodiversity protection. An international coalition formed by non-governmental organizations such as Greenpeace, certain Scandinavian countries, and the G-77 nations (an informal coalition of developing countries that plays a major role in many U.N. decisions and policy processes), has called for the United Nations to establish means of assuring biosafety for the protection of biodiversity, as well as improve the capabilities of developing nations for managing the biotechnological transformation of agriculture so that it is consistent with their agricultural, socioeconomic, and environmental goals and sustainable development. Authority for U.N. enactment of such a legally-binding framework is provided by the 1992 Convention on Biological Diversity.

Convention on Biological Diversity

Biological diversity was raised at the U.N. Conference on the Human Environment held in Stockholm in 1972 and prioritized by the newly formed United Nations Environmental Program (UNEP) in 1973. In 1988, a joint resolution of the U.S. Congress signed by President Reagan lent support to U.S. initiatives for an international agreement, and UNEP convened the first of several expert groups to evaluate the need for (and later, to draft) an international legal instrument, or convention, for the conservation and sustainable use of biological diversity.

In June 1992, the convention was "opened for signature" at the U.N. Conference on Environment and Development in Rio de Janeiro, Brazil, despite displeasure by the United States and France over irregularities in the hasty negotiation process, and legal ambiguities and substantive deficiencies in the final text. By June 1993, 168 nations had signed on, and in late December 1993, the Convention on Biological Diversity (CBD) came into force. Almost 150 of the signatory nations have since ratified the CBD and are thereby subject to it as "parties." The United States, a late and reluctant signatory, has never ratified the CBD, but has been allowed to participate as an observer at the subsequent conferences of the parties and working group meetings. In 1996, the CBD secretariat was installed in Montreal, Canada, with Calestous Juma of Kenya as its executive secretary.

Initially conceived as a framework for preventing "loss of species and equitable sharing of genetic resources," the enacted CBD now stands for more—namely, for ensuring sustainable development, for ensuring that all parties have biosafety procedures, and for building the capabilities of developing nations in biotechnology, biodiversity protection, and associated matters such as biosafety. The CBD is generally regarded as one of the most significant developments in international law for environmental protection and national development.

The CBD is laden with principles, suggestions, and legally ambiguous but potentially obligatory mandates for the party nations. However, to the extent that it obligates party nations, it will also affect their relationships with nonparty nations such as the United States, and thereby have indirect effect on nonparties.

Many provisions call for, in a mixture of obligatory and aspirational terms, actions by parties that will build the biotechnical and biodiversity capabilities of developing nations, such as providing research, training, and financial assistance; engaging in technology transfer; using impact assessment and information sharing; and making equitable arrangements for sharing the fruits of research and commerce involving biodiversity. Several matters that were hotly disputed in drafting the CBD are left unresolved in the final text, which designates them for future resolution. These include intellectual property rights, liability and sanctions, and biosafety.

Two provisions directly address biosafety. Article 19(3) provides that: "The parties shall consider the need for and modalities of a protocol setting out appropriate procedures, including, in particular, advance informed agreement, in the field of the safe transfer, handling, and use of any living modified organism resulting from biotechnology that may have an adverse effect on the conservation and sustainable use of biological diversity."

Article 8(g) calls upon each contracting party, "as far as possible and as appropriate [to] . . . establish or maintain means to regulate, manage, or control the risks associated with the use and release of living modified organisms resulting from biotechnology, which are likely to have adverse environmental impacts that could affect the conservation and sustainable use of biological diversity, taking into account the risks to human health."

These provisions are amplified by Article 19(4), which requires that each party share any available information about its use of and safety regulations for handling LMOs (including potential risks) with any other party.

But other provisions, such as development of a future protocol on biosafety, are substantively related to Article 19(3), and can influence its implementation. For example, Article 16 calls for a cooperative approach to patent rights and technology transfer among the parties. It also calls on the parties to have their private sectors (such as biotechnology companies) similarly cooperate on intellectual property matters and engage in technology transfer. Article 16 further defines the technologies to be transferred as those "that are relevant to the conservation and sustainable use of biological diversity or make use of genetic resources" without causing "significant harm to the environment." Significantly, it also expansively provides that technology includes biotechnology.

Thus, if parties comply with Article 16, developing nations would be able to develop their own capabilities for both biotechnology and biosafety, gaining far more than what would be gained from a prescriptive protocol developed under Article 19. Nevertheless, development of an Article 19 protocol on biosafety now preoccupies the CBD parties, probably because of immediate concerns about environmental risks, the desire to slow down the onslaught of LMOs made in the United States, and the need for time to develop economic and political strategies.

Biosafety Protocol

Parties to the CBD meet annually at a Conference of the Parties (COP), with the United States and numerous nongovernmental organizations permitted to attend as observers. Discussion of a biosafety protocol dominated the first two COPs in 1994 and 1995, and led to the creation of an open-ended ad hoc working group in November 1995 with the mandate to develop a protocol on biosafety. The working group will meet in Arhus, Denmark, in July to take first steps such as defining terms, selecting issues to be addressed, setting the boundaries of the protocol, and reviewing existing biosafety policies.

According to Juma, dates for completion of the protocol have not been fixed, although it is hoped that a draft will be available so that negotiation of a final text can begin in 1998. A consensus decision on the protocol will then be sought at the next COP, with disputed provisions to be negotiated to resolution, following traditional U.N. practice. Thus, a final biosafety protocol could be enacted by 1999.

The working group's mandate is provided by *Decision Document II/5,* approved at the COP-2 meeting held in Jakarta, Indonesia, in November 1995. The mandate sets forth reasons for a protocol including: gaps in knowledge regarding the "inter-

action between LMOs resulting from modern biotechnology and the environment, taking into account the relatively short period of experience with the releases of such organisms, the relatively small number of species and traits used, and the lack of experience in the range of environment . . .;" that existing international agreements do not specifically address the issue of transboundary movements of LMOs; that international action "should offer an effective and efficient framework for . . . insuring biosafety through effective risk assessment and risk management . . .;" and a large majority of the parties favor the development of a protocol on biosafety.

The mandate directs the working group to evaluate existing LMO biosafety policies in developing the protocol, such as guidelines enacted by the United Nations' Food and Agriculture Organization, the Organization for Economic Cooperation and Development (OECD), and most importantly, the International Technical Guidelines on Safety in Biotechnology now being finalized by UNEP.

The UNEP guidelines, based on work done by a U.K.–Dutch team, represent a more flexible, nonbinding approach, which is preferred by the United States and several parties to the CBD. Instead of being fitted with a rigid protocol, each nation would have the opportunity to consider guidelines and ultimately craft its own approach to biosafety.

The mandate provides that finalization of the UNEP guidelines "does not prejudice the development and conclusion of such . . . protocol," and suggests that the guidelines may serve as an interim mechanism during protocol development, as well as a complementary system after completion and adoption of the protocol in order "to facilitate development of national capacities to assess and manage risks, establish adequate information systems, and develop expert human resources." Thus, the working group is directed to consider a parallel biosafety development within the United Nations, one that can accomplish "capacity building" as envisioned by Article 16 of the CBD.

The mandate concludes with the COP-2 decision that the working group is "to seek solution to the abovementioned concerns through a negotiation process to develop. . . a protocol on biosafety, specifically focusing on transboundary movement of any living modified organism resulting from modern biotechnology that may have an adverse effect on the conservation and sustainable use of biological diversity, setting out for consideration, in particular, appropriate procedure for advance informed agreement."

The annex to the decision document contains terms of reference to give more detailed guidance to the working group. According to the annex, priority is to be given to the form and scope of advance informed agreement, the relevant categories of LMOs, the "precautionary principle" contained in UNEP's Rio meeting declaration, completion of the group's work by 1998, and ratification of the protocol by the largest number of parties. The working group is further directed to ensure that the protocol will minimize unnecessary negative impacts on biotechnology research, development, and transfer.

At the July meeting in Arhus, the working group will begin to grapple with protocol development under this complex mandate. A task force of agencies has been formed at the State Department to represent U.S. interests, although the U.S. role will be limited by its observer status. Germany, Japan, the United Kingdom, and the Netherlands, nascent biotechnological powers who are parties to the CBD, also favor the more flexible, nonbinding guidelines approach advocated by the United States.

According to Simon Best, CEO of Zeneca, a biotechnology firm, and chairman of BIO's Committee on Agricultural Biotechnology, "The widely held view of developed nations and many developing countries is to follow a guidelines approach to assure that the most appropriate system can be used in each developing nation, including advance informed agreement and capacity-building procedures, rather than the more inflexible binding protocol approach. Guidelines would allow for the customized adoption of best practices for each nation, and compatibility with its existing laws and infrastructure. Most countries believe this approach would assure a more fully protective approach to be taken in each nation. The protocol effort also has [the] unfortunate potential for diverting COP attention and resources from major needs like sustainable development and preventing deforestation."

Lisa Zannoni of the OECD points out that "many nations use guidelines as the United States uses regulations," and that "the UNEP, FAO, OECD, and other guidelines do not leave many gaps. UNEP is now developing guideline implementation procedures [that] will fill remaining gaps, such as how to define and implement advance informed agreement for commercial transboundary shipments." The OECD has started developing a series of expert consensus documents, state-of-the-art reviews on the environmental biosafety of transgenic plants. Like UNEP and the CBD secretariat, the OECD is providing biosafety information through the Internet for informing the general public in all nations.

Despite these views and guideline enhancement efforts, strong pressure for a legally binding protocol with stringent features, a virtual biosafety regulation template for each nation, is anticipated from the G-77 group of nations, along with China, Sweden, and Denmark, with support from environmental organization observers.

As a result, the working group must grapple with many technical, legal, and policy issues in a volatile political context, such as whether the protocol should be legally binding and require national adoption, or be advisory; if binding, whether it should provide for enforcement, sanctions, and liability; and whether binding or advisory, to what extent it should adopt, or defer to, the biosafety features of UNEP and other guidelines, and the biosafety experience gained in other developed nations.

On the issue of consent, the group must also consider whether the advance informed agreement process should be a simple notification procedure like the prior informed consent procedure used for pesticide exports under various laws and treaties, or more expansive and require, for example, that LMOs intended for shipment meet special testing requirements, be evaluated by a particular method of risk assessment, or be used subject to a particular method of risk management; whether advance informed agreement should be carried out by public officials in each nation or by the private parties arranging for transboundary shipment and, if the latter, how the proprietary information should be safeguarded; and whether the public should be provided with information about the shipment.

In addition, the issue remains whether the protocol should contain features that minimize conflicts with the General Agreement on Tariffs and Trade (GATT) and World Trade Organization, or leave such conflicts to subsequent case-by-case resolution.

The stage is thus set for reaching accord on a biosafety protocol for LMOs. Depending on its features, such a protocol could play a major role in shaping the future use of biotechnology in agriculture, sustainable development in developing nations, and the growth of the biotechnology industry around the world.

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